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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/817,015	03/23/2001	Willem P.C. Stemmer	02-104720US	5728

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MAXYGEN, INC.  
INTELLECTUAL PROPERTY DEPARTMENT  
515 GALVESTON DRIVE  
RED WOOD CITY, CA 94063

EXAMINER
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BYRD, DEVON R

ART UNIT	PAPER NUMBER
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1639

DATE MAILED: 11/12/2003

11

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/817,015

Applicant(s)

STEMMER ET AL.

Examiner

Devon R Byrd

Art Unit

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FILE  
COPY

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 22 September 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-185 is/are pending in the application.
- 4a) Of the above claim(s) 1-73 and 109-185 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 74-108 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

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DETAILED ACTION

*STATUS OF THE APPLICATION*

THE IDS'S OF PAPER NOS.

*STATUS OF THE CLAIMS*

CLAIMS 1-185 ARE PENDING IN THIS APPLICATION AND ARE SUBJECT TO RESTRICTION/ELECTION OF SPECIES. OF THE ABOVE CLAIMS, 1-73 AND 109-185 ARE WITHDRAWN FROM CONSIDERATION AS THEY ARE DIRECTED TO NON-ELECTED GROUPS.

*ELECTION/RESTRICTIONS*

CLAIMS 1-73 AND 109-185 ARE WITHDRAWN FROM FURTHER CONSIDERATION PURSUANT TO 37 CFR 1.142(B) AS BEING DRAWN TO A NONELECTED INVENTION, THERE BEING NO ALLOWABLE GENERIC OR LINKING CLAIM. APPLICANT'S ELECTION OF SPECIES IS ACKNOWLEDGED. THE ABOVE ELECTIONS WERE MADE WITHOUT TRAVERSE IN PAPER NO. 10.

*CLAIM REJECTIONS - 35 USC § 112*

THE FOLLOWING IS A QUOTATION OF THE FIRST PARAGRAPH OF 35 U.S.C. 112:

THE SPECIFICATION SHALL CONTAIN A WRITTEN DESCRIPTION OF THE INVENTION, AND OF THE MANNER AND PROCESS OF MAKING AND USING IT, IN SUCH FULL, CLEAR, CONCISE, AND EXACT TERMS AS TO ENABLE ANY PERSON SKILLED IN THE ART TO WHICH IT PERTAINS, OR WITH WHICH IT IS MOST NEARLY CONNECTED, TO MAKE AND USE THE SAME AND SHALL SET FORTH THE BEST MODE CONTEMPLATED BY THE INVENTOR OF CARRYING OUT HIS INVENTION.

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1. CLAIMS 74-108 ARE REJECTED UNDER 35 USC 112, FIRST PARAGRAPH, AS CONTAINING SUBJECT MATTER WHICH WAS NOT DESCRIBED IN THE SPECIFICATION IN SUCH A WAY AS TO REASONABLY CONVEY TO ONE SKILLED IN THE RELEVANT ART THAT THE INVENTOR(S), AT THE TIME THE APPLICATION WAS FILED, HAD POSSESSION OF THE CLAIMED INVENTION. APPLICANT IS DIRECTED TO THE GUIDELINES FOR THE EXAMINATION OF PATENT APPLICATIONS UNDER THE 35 USC 112, ¶ 1 "WRITTEN DESCRIPTION" REQUIREMENT, FEDERAL REGISTER, VOL. 66, NO. 4 PAGES 1099-1111, FRIDAY JANUARY 5, 2001. THIS IS A WRITTEN DESCRIPTION REJECTION.

THESE CLAIMS ENCOMPASS A BROAD GENUS. THE CLAIMS ARE DRAWN TO THE USE OF ANY NUCLEIC ACID LIBRARY (OR LIBRARIES) IN ANY METHOD TRANSFORMATION OF ANY RECIPIENT CELL, ORGANELLE (OR ORGANISM COMPRISING A RECIPIENT CELL), THAT RESULTS IN ANY EFFECT UPON ANY PHENOTYPE, WHEREIN THE STRUCTURE OF THE NUCLEIC ACIDS USED TO MAKE THE LIBRARY AND THE OPERATIVE LINKAGE BETWEEN A MEMBER (OR MEMBERS) OF SAID LIBRARY AND THE EFFECT IT MAY HAVE ON A "COMPLEX PHENOTYPE" ARE UNDEFINED. CONSEQUENTLY, THE SCOPE OF THESE CLAIMS IS ENORMOUS BECAUSE THEY WOULD INCLUDE AN INFINITE NUMBER OF METHODS FOR PRODUCING AN INFINITE NUMBER OF STRUCTURAL VARIANTS (I.E., LIBRARY MEMBERS) WHEREIN NO DISTINGUISHING STRUCTURAL ATTRIBUTES ARE PROVIDED FOR THE NUCLEIC ACIDS, LIBRARIES, OR RECIPIENT ENTITIES THAT ARE COMBINED TOGETHER TO FORM THE PRODUCT THAT EFFECTS THE METHOD OF "CONTROLLING A COMPLEX PHENOTYPE".

THE SPECIFICATION AND CLAIMS DO NOT PLACE ANY LIMIT ON THE NUMBER OF NUCLEIC ACID SEGMENTS, THE SEQUENCES OF SAID NUCLEIC ACID SEGMENTS, OR THE PROTEINS THAT MIGHT BE ENCODED BY SAID NUCLEIC ACIDS COMPRISING THESE LIBRARY MEMBERS. NEITHER ARE THERE ANY LIMITATIONS AS TO THE NUMBER AND TYPE(S) OF "COMPLEX PHENOTYPE(S)", NOR THE MANNER IN WHICH SAID PHENOTYPES MIGHT BE CONTROLLED. ALTHOUGH THE SPECIFICATION DISCLOSES THREE PROPHETIC EXAMPLES (SEE SPECIFICATION, PAGES 57-64), THE

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SPECIFICATION AND CLAIMS DO NOT PROVIDE ANY GUIDANCE AS TO WHAT STRUCTURAL FEATURES ALL OF THE COMPOUNDS FOR USE WITH METHODS OF THE CLAIMED INVENTION MIGHT SHARE. PROVIDING PROPHETIC EXAMPLES DIRECTED TO "GENERIC" CLASSES OF COMPOUNDS THAT MIGHT POTENTIALLY RELATE TO "EXPLORING OIL PHENOTYPE SPACE" DOES NOT SUFFICIENTLY DESCRIBE COMPOUNDS THAT DO NOT FALL WITHIN THE "OIL PHENOTYPE SPACE" CLASS AND SUBCLASS (PLEASE NOTE: BECAUSE "COMPLEX PHENOTYPE" READS ON ANY BIOLOGIC LEVEL OF ORGANIZATION (I.E., CATION CONCENTRATION, METABOLITE COMPOSITION AND/OR CONTENT, CELLULAR STRUCTURE AND/OR FUNCTION, TISSUE STRUCTURE AND/OR FUNCTION, ORGAN STRUCTURE AND/OR FUNCTION, ETC.), APPLICANTS' CLAIMS WOULD ENCOMPASS AN INFINITE NUMBER OF COMPOUNDS IN VIRTUALLY EVERY CLASS AND SUBCLASS). THE SPECIFICATION DOES NOT DESCRIBE ANY SPECIFIC COMPOUNDS OTHER THAN THOSE THAT ARE DISCLOSED IN THE SPECIFICATION. CONSEQUENTLY, THERE IS NO TEACHING THAT WOULD ALLOW A PERSON OF SKILL IN THE ART TO DETERMINE *A PRIORI* THAT APPLICANTS WERE IN POSSESSION OF THE FULL SCOPE OF THE CLAIMED INVENTION AT THE TIME OF FILING BECAUSE THERE IS NO COMMON STRUCTURAL ATTRIBUTES THAT CAN LINK TOGETHER ALL OF THE CLAIMED COMPOUNDS.

THE GENERAL KNOWLEDGE AND LEVEL OF SKILL IN THE ART DO NOT SUPPLEMENT THE OMITTED DESCRIPTION BECAUSE SPECIFIC, NOT GENERAL, GUIDANCE IS WHAT IS NEEDED. SINCE THE DISCLOSURE FAILS TO DESCRIBE THE COMMON ATTRIBUTES OR CHARACTERISTICS THAT IDENTIFY ALL OF THE MEMBERS OF THE GENUS OR EVEN A SUBSTANTIAL PORTION THEREOF, AND BECAUSE THE GENUS IS ENORMOUS AND HIGHLY VARIANT, LISTING PROPHETIC EXAMPLES LIKE "EXPLORING OIL PHENOTYPE SPACE" IS INSUFFICIENT TO TEACH THE ENTIRE GENUS. CONSEQUENTLY, ONE OF SKILL IN THE ART WOULD REASONABLY CONCLUDE THAT THE DISCLOSURE FAILS TO PROVIDE A REPRESENTATIVE NUMBER OF SPECIES TO DESCRIBE THIS ENORMOUS GENUS. THUS, APPLICANT WAS NOT IN POSSESSION OF THE CLAIMED GENUS.

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WITH REGARD TO THE DESCRIPTION REQUIREMENT, APPLICANTS' ATTENTION IS DIRECTED TO THE COURT OF APPEALS FOR THE FEDERAL CIRCUIT WHICH HELD THAT A "WRITTEN DESCRIPTION OF AN INVENTION INVOLVING A CHEMICAL GENUS, LIKE A DESCRIPTION OF A CHEMICAL SPECIES, 'REQUIRES A PRECISE DEFINITION, SUCH AS BY STRUCTURE, FORMULA [OR] CHEMICAL NAME,' OF THE CLAIMED SUBJECT MATTER SUFFICIENT TO DISTINGUISH IT FROM OTHER MATERIALS."

*UNIVERSITY OF CALIFORNIA V. ELI LILLY AND Co.*, 43 USPQ2d 1398, 1405 (1997), QUOTING *FIER'S V. REVEL*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (BRACKETED MATERIAL IN ORIGINAL) [THE CLAIMS AT ISSUE IN *UNIVERSITY OF CALIFORNIA V. ELI LILLY* DEFINED THE INVENTION BY FUNCTION OF THE CLAIMED DNA (ENCODING INSULIN)].

ALTHOUGH DIRECTED TO DNA COMPOUNDS, THIS HOLDING WOULD BE DEEMED TO BE APPLICABLE TO A GENERIC OF COMPOUNDS- WHICH REQUIRES A REPRESENTATIVE SAMPLE OF COMPOUNDS AND/OR A SHOWING OF SUFFICIENT IDENTIFYING CHARACTERISTICS- TO DEMONSTRATE POSSESSION OF THE COMPOUND OR GENERIC(S). FOR EXAMPLE, IN A RECENT COURT CASE IN LINE WITH *ELI LILLY*, JUDGE LOURIE WRITING FOR THE CAFC MADE THE FOLLOWING OBSERVATION:

"A DESCRIPTION OF AN ANTI-INFLAMMATORY STEROID, I.E., A STEROID (A GENERIC STRUCTURAL TERM) HAVING THE FUNCTION OF LESSENING INFLAMMATION OF TISSUES, FAILS TO DISTINGUISH ANY STEROID FROM OTHERS HAVING THE SAME ACTIVITY OR FUNCTION. SIMILARLY, THE EXPRESSION "AN ANTIBIOTIC PENICILLIN" FAILS TO DISTINGUISH A PARTICULAR PENICILLIN MOLECULE FROM OTHERS POSSESSING THE SAME ACTIVITY. "

SEE: J. LOURIE DECISION IN *ENZO BIOCHEM, INC. V. GEN-PROBE INC. ET AL.* No. 01-1230 (CAFC: DECIDED APRIL 2, 2002) (CITATION FORTHCOMING).

IN THIS REGARD, APPLICANT IS REFERRED TO THE SEMINAL CASE OF *UNIVERSITY OF CALIFORNIA V. ELI LILLY & Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) AND THE "GUIDELINES FOR EXAMINATION OF PATENT APPLICATIONS UNDER THE 35 USC 112, FIRST

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PARAGRAPH, 'WRITTEN DESCRIPTION' REQUIREMENT" PUBLISHED IN 1242 OG 168-178 (JANUARY 30, 2001).

IT IS NOTED THAT WRITTEN DESCRIPTION IS LEGALLY DISTINCT FROM ENABLEMENT:

"ALTHOUGH THE TWO CONCEPTS OF ARE ENTWINED, THEY ARE DISTINCT AND EACH IS EVALUATED UNDER SEPARATE LEGAL CRITERIA. THE WRITTEN DESCRIPTION REQUIREMENT, A QUESTION OF FACT, ENSURES THAT THE INVENTOR CONVEYS TO OTHERS THAT HE OR SHE HAD POSSESSION OF THE CLAIMED INVENTION; WHEREAS, THE ENABLEMENT REQUIREMENT, A QUESTION OF LAW, ENSURES THAT THE INVENTOR CONVEYS TO OTHERS HOW TO MAKE AND USE THE CLAIMED INVENTION." SEE 1242 OG 169 (JANUARY 30, 2001) CITING *UNIVERSITY OF CALIFORNIA V. ELI LILLY & CO.*

***CLAIM REJECTIONS - 35 USC § 102***

THE FOLLOWING IS A QUOTATION OF THE APPROPRIATE PARAGRAPHS OF 35 U.S.C. 102 THAT FORM THE BASIS FOR THE REJECTIONS UNDER THIS SECTION MADE IN THIS OFFICE ACTION:

A PERSON SHALL BE ENTITLED TO A PATENT UNLESS -

(B) THE INVENTION WAS PATENTED OR DESCRIBED IN A PRINTED PUBLICATION IN THIS OR A FOREIGN COUNTRY OR IN PUBLIC USE OR ON SALE IN THIS COUNTRY, MORE THAN ONE YEAR PRIOR TO THE DATE OF APPLICATION FOR PATENT IN THE UNITED STATES.

CLAIMS 74-107 ARE REJECTED UNDER 35 U.S.C. 102(B) AS BEING ANTICIPATED BY WO 97/20078, PUBLISHED JUNE 5, 1997 (HEREINAFTER REFERRED TO AS '078).

'078 TEACHES A METHOD FOR CONTROLLING A COMPLEX PHENOTYPE COMPRISING:

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- PROVIDING A LIBRARY OF NUCLEIC ACIDS COMPRISING ONE OR MORE POLYNUCLEOTIDE SEGMENTS OPERABLY LINKED TO AT LEAST ONE TRANSCRIPTION REGULATORY SEQUENCE (P 99, LN 32- P 100, LN 2);
- INTRODUCING THE LIBRARY OF NUCLEIC ACIDS INTO A PLURALITY OF RECIPIENT CELLS OR INTRACELLULAR ORGANELLES, WHEREBY SUBSETS OF TWO OR MORE MEMBERS OF THE LIBRARY, WHICH SUBSETS ALTER EXPRESSION OR ACTIVITY OF ONE OR MORE COMPONENTS OF A MULTIGENIC PHENOTYPE (P 98, LNS 5-8), ARE INTRODUCED INTO A PLURALITY OF THE RECIPIENT CELLS OR ORGANELLES (SEE FIGS. 25-30); AND
- IDENTIFYING AT LEAST ONE RECIPIENT CELL, INTRACELLULAR ORGANELLE OR ORGANISM COMPRISING A RECIPIENT CELL, WITH A DESIRED PHENOTYPE (P 51, LNS 34-37);
- WHEREIN THE LIBRARY COMPRISES RANDOM POLYNUCLEOTIDE SEGMENTS (P 10, LNS 5-21);
- WHEREIN THE LIBRARY COMPRISES PRE-SELECTED POLYNUCLEOTIDE SEGMENTS (P 17, LNS 21-26) BY
  - INTRODUCING A POPULATION OF RANDOM OR SELECTED POLYNUCLEOTIDE SEGMENTS INTO A PLURALITY OF RECIPIENT CELLS, (B) SELECTING AT LEAST ONE RECIPIENT CELL, INTRACELLULAR ORGANELLE, OR ORGANISM COMPRISING A RECIPIENT CELL, WITH A DESIRED PHENOTYPE, AND (C) RECOVERING ONE OR MORE POLYNUCLEOTIDE SEGMENTS FROM THE AT LEAST ONE RECIPIENT CELL WITH A DESIRED PHENOTYPE, THEREBY PRE-SELECTING ONE OR MORE POLYNUCLEOTIDE SEGMENTS (P 8, LN 5- P 9, LN 9),
  - WHEREIN THE POLYNUCLEOTIDE SEGMENTS ARE PRE-SELECTED FOR ONE OR MORE ENCODED ACTIVITIES (P9, LNS 4-9), AND WHEREIN



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- THE PRE-SELECTED POLYNUCLEOTIDE SEGMENTS ARE IDENTIFIED BY COMPUTATIONAL ANALYSIS OF AT LEAST ONE GENOMIC OR EXPRESSED SEQUENCE (P 17, LNS 2-8),
  - THE PRE-SELECTED POLYNUCLEOTIDE SEGMENTS ARE IDENTIFIED USING AT LEAST ONE cDNA OR OLIGONUCLEOTIDE ARRAY (P 66, LNS 9-14),
  - THE PRE-SELECTED POLYNUCLEOTIDE SEGMENTS ARE IDENTIFIED BY METABOLIC MODELING AND FLUX ANALYSIS (P 25, LNS 6-16, AND P 102, LNS 1-11)
  - THE PRE-SELECTED POLYNUCLEOTIDE SEGMENTS ARE IDENTIFIED BY SCREENING OR SELECTING ENCODED PEPTIDES (P 7, LN 33- P 8, LN 4),
  - THE PRE-SELECTED POLYNUCLEOTIDE SEGMENTS ARE IDENTIFIED BY FLOW CYTOMETRY (P 159, LN 36- P 160, LN 5),
  - THE PRE-SELECTED POLYNUCLEOTIDE SEGMENTS ARE IDENTIFIED BY YEAST TWO-HYBRID ANALYSIS (P 79, LNS 20-30),
  - THE PRE-SELECTED POLYNUCLEOTIDE SEGMENTS COMPRISE ONE OR MORE ELEMENTS OF A SINGLE OR MULTIPLE METABOLIC OR GENETIC PATHWAY(S) (P 25, LNS 6-16),
- ⊙ WHEREIN THE PHENOTYPE (P 98 LNS 1-4) IS REGULATED BY AT LEAST ONE EPIGENETIC MECHANISM (P 7, LN 33- P 8, LN 4; P 98 LNS 1-36),
  - WHEREIN THE EPIGENETIC MECHANISM IS CHROMATIN SILENCING, REGULATION BY CYTOPLASMIC FACTORS, ANTISENSE SUPPRESSION, PROMOTER ALTERATION, POST-TRANSCRIPTIONAL GENE SILENCING, AND DNA RECOMBINATION; WHEREIN THE POST-TRANSCRIPTIONAL GENE SILENCING IS BY A TRANSDOMINANT INHIBITOR (P 98, LNS 5-27),

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- WHEREIN THE POLYNUCLEOTIDE SEGMENTS COMPRISE A GENOMIC DNA, A SENSE-STRAND DNA, AN ANTISENSE DNA, A DNA ENCODING A DOMINANT NEGATIVE PROTEIN VARIANT OR A TRANSDOMINANT PROTEIN VARIANT, A DNA ENCODING A PEPTIDE MODULATOR, A DNA ENCODING A 5-100 AMINO ACID PEPTIDE, AN RNA, A SENSE-STRAND RNA, AN ANTISENSE RNA (P 98, LNS 1-36: APPLICANT'S ATTENTION IS SPECIFICALLY DIRECTED TO LNS 1-4 AND THE LIST OF GENES INVOLVED IN CONJUGATIVE DNA TRANSFER DELINEATED IN LNS 9-16), A VECTOR (EPISOMAL OR OTHERWISE) (P 98, LNS 18-27)
- WHEREIN THE VECTOR IS A PLASMID (P 89, LN 19- P90, LN 9), A BACTERIOPHAGE, A VIRUS (P92, LNS 18-31), A PROVIRUS, A BAC, A YAC, A TRANSPOSON, OR A PHAGEMID (P46, LNS 17-27),
- WHEREIN THE RECIPIENT CELLS COMPRISE A BACTERIUM, A YEAST, AN ANIMAL CELL (P 19, LNS 18-31), OR PLANT CELL (P97, LNS 34-36),
- WHEREIN THE COMPLEX PHENOTYPE IS PROTEIN CONTENT OR COMPOSITION (P 98, LNS 1-4),
- WHEREIN CONTROLLING THE PHENOTYPE COMPRISES MODULATING ACTIVITY OF ONE OR MORE TARGETS (P 71, LNS 9-18),
  - WHEREIN THE ONE OR MORE TARGETS COMPRISE ONE OR MORE ENZYMES (P 98, LNS 1-16),
- COMPRISING IDENTIFYING OR RECOVERING ONE OR MORE MEMBERS OF THE LIBRARY FROM THE CELLS WITH A DESIRED PHENOTYPE IDENTIFIED IN STEP (III) (P 91, LNS 21-35),
  - RECOMBINING OR MUTATING THE ONE OR MORE IDENTIFIED OR RECOVERED MEMBERS OF THE LIBRARY, THEREBY PRODUCING AT LEAST ONE RECOMBINANT POLYNUCLEOTIDE SEGMENT (P 91, LNS 21-35),

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- O RECURSIVELY RECOMBINING OR MUTATING THE ONE OR MORE MEMBERS OF THE LIBRARY (P 99, LNS 14-18),
- O INTRODUCING THE AT LEAST ONE RECOMBINANT POLYNUCLEOTIDE SEGMENT INTO A HOST CELL (P99, LNS 32-36),
- O INTEGRATING AT LEAST ONE RECOMBINANT POLYNUCLEOTIDE SEGMENT INTO A CHROMOSOME (P 100, LNS 21-24),
- O REGENERATING AT LEAST ONE MULTICELLULAR ORGANISM COMPRISING THE HOST CELL (P 97, LN 34- P 98, LN 4),
- O WHEREIN THE HOST CELL IS A BACTERIAL CELL, A FUNGAL CELL, A PLANT CELL OR AN ANIMAL CELL (P 19, LNS 18-31), OR PLANT CELL (P97, LNS 34-36),
- O WHEREIN AT LEAST ONE GENETIC ELEMENT CORRESPONDING TO A LIBRARY MEMBER OR RECOMBINANT POLYNUCLEOTIDE SEGMENT IS ISOLATED (P 55, LNS 1-4),
- O FURTHER COMPRISING: RECOMBINING OR MUTATING THE AT LEAST ONE ISOLATED GENETIC ELEMENT, THEREBY PRODUCING A LIBRARY OF ISOLATED GENE HOMOLOGUES, AND SELECTING AT LEAST ONE GENE HOMOLOGUE WITH A DESIRED PROPERTY (P 55, LNS 4-8).

THEREFORE, ALL OF THE CLAIMED LIMITATIONS DISCUSSED ABOVE HAVE BEEN ANTICIPATED BY '078.

CLAIMS 74, 75, 77, 79, 82, 86, 87, 89, 91-100, 102, 103, 105, 106, AND 108 ARE REJECTED UNDER 35 U.S.C. 102(B) AS BEING ANTICIPATED BY JOHNSTON ET AL., SCIENCE 240:1538-1541, 1988.

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JOHNSTON TEACHES A METHOD OF CONTROLLING A COMPLEX PHENOTYPE COMPRISING:

- PROVIDING A LIBRARY OF NUCLEIC ACIDS COMPRISING ONE OR MORE POLYNUCLEOTIDE SEGMENTS OPERABLY LINKED TO AT LEAST ONE TRANSCRIPTION REGULATORY SEQUENCE;
- INTRODUCING THE LIBRARY OF NUCLEIC ACIDS INTO A PLURALITY OF RECIPIENT CELLS OR INTRACELLULAR ORGANELLES, WHEREBY SUBSETS OF TWO OR MORE MEMBERS OF THE LIBRARY, WHICH SUBSETS ALTER EXPRESSION OR ACTIVITY OF ONE OR MORE COMPONENTS OF A MULTIGENIC PHENOTYPE, ARE INTRODUCED INTO A PLURALITY OF THE RECIPIENT CELLS OR ORGANELLES;
- IDENTIFYING AT LEAST ONE RECIPIENT CELL, INTRACELLULAR ORGANELLE OR ORGANISM COMPRISING A RECIPIENT CELL, WITH A DESIRED PHENOTYPE (P 1539, COL 1, BOTTOM PARAGRAPH- COL 2 SECOND PARAGRAPH);
- WHEREIN THE POLYNUCLEOTIDE SEGMENTS ARE PRE-SELECTED FOR ONE OR MORE ENCODED ACTIVITIES (P 1538, ABSTRACT, LNS 3-6);
- COMPRISING IDENTIFYING THE PRE-SELECTED POLYNUCLEOTIDE SEGMENTS BY METABOLIC MODELING AND FLUX ANALYSIS (P 1538- 1539, BRIDGING PARAGRAPH);
- WHICH PRE-SELECTED POLYNUCLEOTIDE SEGMENTS COMPRISE ONE OR MORE ELEMENTS OF A SINGLE OR MULTIPLE METABOLIC OR GENETIC PATHWAYS (P 1538- 1539, BRIDGING PARAGRAPH, AND P 1539, COL 3, LNS 3-15);
- WHEREIN THE PHENOTYPE IS REGULATED BY AT LEAST ONE EPIGENETIC MECHANISM (P 1538, COL 3, LNS 31-36);
- WHEREIN THE POLYNUCLEOTIDE SEGMENTS COMPRISE ONE OR MORE OF: A GENOMIC DNA, A cDNA, A SENSE-STRAND DNA, AN ANTISENSE DNA, A DNA ENCODING A DOMINANT NEGATIVE PROTEIN VARIANT OR A TRANSDOMINANT PROTEIN VARIANT, A DNA ENCODING A PEPTIDE MODULATOR, A DNA ENCODING A 5-100 AMINO ACID PEPTIDE, A DNA OR RNA

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DECOY, A VIRAL DNA OR RNA, AN RNA, A SENSE-STRAND RNA, AN ANTISENSE RNA, A tRNA, A RIBOZYME, AN RNP, AND A COMPONENT OF THE RNA SPLICING MACHINERY, WHEREIN THE NUCLEIC ACIDS FURTHER COMPRISE A VECTOR, WHEREIN THE VECTOR COMPRISES AN EPISOMAL VECTOR, WHICH VECTOR IS A PLASMID, A VIRUS, A PROVIRUS, A BAC, A YAC, A TRANSPOSON, A BACTERIOPHAGE, OR A PHAGEMID (P 1539, COL 1, LN 9- COL 2, LN 1);

- WHEREIN THE RECIPIENT CELLS COMPRISE A BACTERIUM, A YEAST, A FUNGUS, A PLANT CELL, OR AN ANIMAL CELL (P 1538, TITLE OF ARTICLE);
- WHEREIN THE PHENOTYPE IS SELECTED FROM AMONG: OIL CONTENT OR COMPOSITION, FAT CONTENT OR COMPOSITION, SUGAR CONTENT OR COMPOSITION, STARCH CONTENT OR COMPOSITION, PROTEIN CONTENT OR COMPOSITION, PHYTOCHEMICAL CONTENT OR COMPOSITION, NUTRACEUTICAL CONTENT OR COMPOSITION, YIELD, TIME TO MATURITY, GROWTH RATE, HEIGHT AT MATURITY, CARBON-FIXATION RATE, SALT-TOLERANCE, HEAT TOLERANCE, COLD TOLERANCE, DROUGHT TOLERANCE, WATER-TOLERANCE, HEAVY METAL TOLERANCE, RADIATION TOLERANCE, RESISTANCE TO A CHEMICAL COMPOSITION, DISEASE RESISTANCE, INSECT RESISTANCE, PARASITE RESISTANCE, COLOR, FLUORESCENCE, HEIGHT, WEIGHT, DENSITY, TOXICITY, FLAVOR, SWEETNESS, BITTERNESS, NUTRITIONAL ACTIVITY, OR THERAPEUTIC ACTIVITY, WHEREIN CONTROLLING THE PHENOTYPE COMPRISES MODULATING ACTIVITY OF ONE OR MORE TARGETS, WHEREIN THE ONE OR MORE TARGETS COMPRISE ONE OR MORE ENZYMES (P 1538, COL 3, LN 17- P 1539, COL 3, LN 15; AND P 1540, COL 2, LNS 17-23);
- FURTHER COMPRISING IDENTIFYING OR RECOVERING ONE OR MORE MEMBERS OF THE LIBRARY FROM THE CELLS WITH A DESIRED PHENOTYPE (P 1539- 1540, BRIDGING PARAGRAPH);

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- FURTHER COMPRISING RECOMBINING OR MUTATING THE ONE OR MORE IDENTIFIED OR RECOVERED MEMBERS OF THE LIBRARY, THEREBY PRODUCING AT LEAST ONE RECOMBINANT POLYNUCLEOTIDE SEGMENT (P 1539, COL 1, LNS 9-29; FIGURE 1; AND P 1539- 1540, BRIDGING PARAGRAPH);
- FURTHER COMPRISING INTRODUCING THE AT LEAST ONE RECOMBINANT POLYNUCLEOTIDE SEGMENT INTO A HOST CELL (P 1539, COL 2, LNS 1-27);
- WHEREIN THE AT LEAST ONE RECOMBINANT POLYNUCLEOTIDE SEGMENT IS INTEGRATED INTO A CHROMOSOME (P 1540, COL 1, LNS 10-25);
- WHEREIN THE HOST CELL IS A BACTERIAL CELL, A FUNGAL CELL, A PLANT CELL OR AN ANIMAL CELL (P 1538, TITLE OF ARTICLE);
- FURTHER COMPRISING ISOLATING AT LEAST ONE GENETIC ELEMENT CORRESPONDING TO A LIBRARY MEMBER OR RECOMBINANT POLYNUCLEOTIDE SEGMENT (P 1540, FIGURE 2);
- WHEREIN THE INTRACELLULAR ORGANELLE COMPRISES A MITOCHONDRIA OR A CHLOROPLAST (P 1538, TITLE OF ARTICLE).

THEREFORE, ALL OF THE CLAIMED LIMITATIONS DISCUSSED ABOVE HAVE BEEN ANTICIPATED BY JOHNSTON ET AL.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DEVON R BYRD WHOSE TELEPHONE NUMBER IS 703-305-0159. THE EXAMINER CAN NORMALLY BE REACHED ON MON-FRI 8A-5P.

IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, ANDREW WANG CAN BE REACHED ON 703-306-2317. THE FAX PHONE NUMBER FOR THE ORGANIZATION WHERE THIS APPLICATION OR PROCEEDING IS ASSIGNED IS 703-308-2742.

APPLICATION/CONTROL NUMBER: 09/817,015

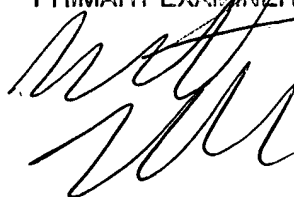
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ART UNIT: 1639

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR  
PROCEEDING SHOULD BE DIRECTED TO THE RECEPTIONIST WHOSE TELEPHONE NUMBER IS 703-  
308-1235.

DB  
NOVEMBER 10, 2003

BENNETT CELSA  
PRIMARY ENGINEER

A handwritten signature in black ink, appearing to read 'Bennett Celsa', written over the printed name and title.